REMARKS

1. Support for the Amendments and New Claims

The specification has been amended to update the cross-reference section in conformance with 37 C.F.R. § 1.78. Such amendments do not constitute new matter.

Support for the amendments to claim 30 and for new claims 44-65 may be found throughout the specification (for example, page 31, line 14 to page 34, line 28), and in particular from page 68, line 16 through page 72, line 12. Thus the amendments and new claims do not constitute new matter.

2. Drawings

The Applicants acknowledge the draftsperson's report and have enclosed herewith a set of formal drawings.

3. Provisional Obviousness-Type Double Patenting

The Examiner has provisionally rejected claim 30 under the doctrine of obviousness-type double patenting as being unpatentable over claims 24 of copending Application No. 09/724,376 (Attorney Docket No. 97-022-B2). The Applicants acknowledge this rejection and will address it when the the claims are otherwise allowable.

4. Claim Rejections – 35 USC § 112, Second Paragraph

The Examiner has rejected claim 30 under 35 U.S.C. § 112, second paragraph under the assertion that it is indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Applicants respectfully traverse, but have nonetheless amended claim 30 obviate the rejection. Therefore, the Applicants respectfully request the Examiner reconsider and withdraw the rejection of claim 30 under 35 U.S.C. § 112, second paragraph.

5. Claim Rejections – 35 USC § 102

The Examiner has rejected claim 30 under 35 U.S.C. § 102(b) under the assertion that it is anticipated by Akong et al. (U.S. Patent No. 5,670,113). The Applicants respectfully traverse this assertion, but have nonetheless amended claim 30 to obviate the rejection.

In order to serve as a proper anticipatory reference, the reference in question must teach each and every claim limitation. Akong et al. teaches apparatus and methods for automated drug screening in which cytoplasmic fluorescence is monitored in response to various agents that may affect intracellular ion levels. The change in intracellular ion concentration is monitored by changes in fluorescence intensity of an ion-sensitive fluorescent indicator in the cytoplasm of the test cells.

The cited reference does not teach or suggest the machine readable storage medium recited in currently pending claim 30. Specifically, Akong does not teach or suggest a machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to execute procedures for detecting the distribution of one or more cellular macromolecule of interest between two or more different cellular compartments on or in individual cells.

Furthermore, Akong neither teaches nor suggests the limitations of claim 30 (a) – (f). Thus, as Akong does not teach or suggest the limitations of claim 30 or the new dependent claims, it cannot serve as a proper anticipatory reference. Therefore the Applicants respectfully request the Examiner reconsider and withdraw the rejections under 35 U.S.C. § 102(b).

6. Claim Rejections – 35 USC § 103

The Examiner has rejected claim 30 under 35 U.S.C. § 103(a) under the assertion that it is unpatentable over Akong et al. in view of Lee et al. (U.S. Patent No. 5,627,908). The Applicants respectfully traverse this assertion, but have nonetheless amended claim 30 to obviate the rejection.

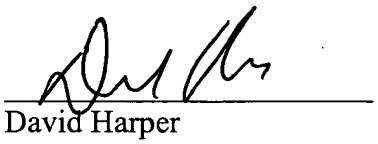
In order to establish a *prima facie* case of obviousness, the cited references much teach or suggest all the claim limitations. For the reasons discussed above, Akong does not teach or suggest all the claim limitations of the present applications. These deficiencies are in no way cured by Lee, which teaches apparatus and methods for a dynamic normalization of cytological

specimens on slides. The combination of Akong and Lee neither teaches nor suggests the machine readable storage medium of claim 30, nor of any of the new dependent claims. Thus Lee does not cure the deficiencies of Akong. As the combination of Akong and Lee does not teach or suggest all the claim limitations of the instant invention, a *prima facie* case of obviousness cannot be established. Hence the Applicants respectfully request the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned attorney at (312) 913-2106.

Respectfully Submitted,

Date: November 13, 2002

By: 

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APPENDIX 1: MARKED-UP VERSION OF AMENDMENTS

In the specification:

On page 1, please replace the paragraph entitled "Cross Reference" (lines 7-11) with the following:

This application is a continuation-in-part of U.S. Applications for Patent S/N 08/810983, filed on February 27, 1997, now U.S. Patent No. 5,989,835 and S/N 08/865,341 filed on May 29, 1997, now U.S. Patent No. 6,103,479; PCT Application WO 97/45730 filed May 29, 1997, and ~~a continuation-in-part of~~claims priority to U.S. Provisional Applications filed December 11, 1997, serial numbers 60/069,246 and 60/069,329 ~~(97,022-A and 97,223-A), serial numbers to be assigned~~.

In the claims:

Please amend the claims as follows:

30. (Amended) A machine readable storage medium comprising a program containing a set of instructions for causing a cell screening system to execute procedures for detecting the distribution of one or more cellular macromolecule of interest between two or more different cellular compartments on and/or in individual cells comprising:

a) scanning multiple cells in an array of locations which contain multiple cells to obtain fluorescent signals from fluorescent reporter molecules on and/or in the cells, wherein the cells possess at least a first fluorescent reporter molecule to identify individual cells, at least a second fluorescent reporter molecule to report on one or more cellular macromolecule of interest, at least a third fluorescent reporter molecule to report on one of the two or more cellular compartments on or in the individual cells, and optionally an at least fourth fluorescent reporter molecule to report on one of the two or more cellular compartments on and/or in the individual cells; wherein the fluorescent signals from the at least first fluorescent reporter

molecule, the at least second fluorescent reporter molecule, the at least third fluorescent reporter molecule, and the at least fourth fluorescent reporter molecule are optically distinguishable;

b) identifying individual cells from the fluorescent signals from the at least first fluorescent reporter molecule;

c) creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells from the fluorescent signals from the at least first fluorescent reporter molecule, the at least second fluorescent reporter molecule, the at least third fluorescent reporter molecule, and/or the at least fourth fluorescent reporter molecule;

d) determining an intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells in response to contacting the cells with a test stimulus;

e) comparing the intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells in response to contacting the cells at a first time point with a test stimulus to:

i) an intensity of fluorescent signals of the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells in response to contacting the cells with the test stimulus from at least a second time point; and/or

ii) an intensity of fluorescent signals from the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells that have not been contacted with the test stimulus; and

f) determining the effect of the test stimulus on the distribution of the one or more cellular macromolecule of interest between the two or more different cellular compartments on and/or in the individual cells as a function of the intensity of the fluorescent signals of the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells.~~identifying novel receptor agonists and antagonists, wherein the cell screening system comprises a high magnification fluorescence optical system with a stage adapted for holding cells and a means for moving the stage, a digital~~

~~camera, a light source for receiving and processing the digital data from the digital camera, and a computer means for receiving and processing the digital data from the digital camera.~~

44. (New) The machine readable storage medium of claim 30, wherein the at least first fluorescent reporter molecule identifies nuclei, and wherein the identifying of the individual cells comprises identifying the nucleus of the individual cells.

45. (New) The machine readable storage medium of claim 44, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cytoplasmic mask from the fluorescent signals from the at least first fluorescent reporter molecule.

46. (New) The machine readable storage medium of claim 45, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cell membrane mask from the fluorescent signals from the at least third fluorescent reporter molecule.

47. (New) The machine readable storage medium of claim 46, wherein the intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the cytoplasmic mask and the cell membrane mask on and/or in the individual cells is determined.

48. (New) The machine readable storage medium of claim 44, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cytoplasmic mask from the fluorescent signals from the at least second fluorescent reporter molecule.

49. (New) The machine readable storage medium of claim 48, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cell membrane mask from the fluorescent signals from the at least third fluorescent reporter molecule.

50. (New) The machine readable storage medium of claim 49, wherein the intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the cytoplasmic mask and the cell membrane mask on and/or in the individual cells is determined.

51. (New) The machine readable storage medium of claim 44, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cytoplasmic mask from the fluorescent signals from the at least third fluorescent reporter molecule.

52. (New) The machine readable storage medium of claim 51, wherein the cell possess the at least fourth fluorescent reporter molecule and wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a cell membrane mask from the fluorescent signals from the at least fourth fluorescent reporter molecule.

53. (New) The machine readable storage medium of claim 52, wherein the intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the cytoplasmic mask and the cell membrane mask on and/or in the individual cells is determined.

54. (New) The machine readable storage medium of claim 47, wherein the procedures further comprise determining a ratio of integrated intensity of the fluorescent signals from the at least second fluorescent reporter molecule between the cytoplasmic mask and the cell membrane mask on and/or in the multiple cells.

55. (New) The machine readable storage medium of claim 50, wherein the procedures further comprise determining a ratio of integrated intensity of the fluorescent signals from the at least second fluorescent reporter molecule between the cytoplasmic mask and the cell membrane mask on and/or in the multiple cells.

56. (New) The machine readable storage medium of claim 53, wherein the procedures further comprise determining a ratio of integrated intensity of the fluorescent signals from the at least second fluorescent reporter molecule between the cytoplasmic mask and the cell membrane mask on and/or in the multiple cells.

57. (New) The machine readable storage medium of claim 44, wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating an endoplasmic reticulum mask from the fluorescent signals from the at least third fluorescent reporter molecule.

58. (New) The machine readable storage medium of claim 57, wherein the cell possess the at least fourth fluorescent reporter molecule and wherein the creating a mask of each of the two or more cellular compartments of interest on and/or in the individual cells comprises creating a Golgi apparatus mask from the fluorescent signals from the at least fourth fluorescent reporter molecule.

59. (New) The machine readable storage medium of claim 58, wherein the intensity of the fluorescent signals from the at least second fluorescent reporter within the endoplasmic reticulum mask and the Golgi apparatus masks on and/or in the individual cells is determined.

60. (New) The machine readable storage medium of claim 59, wherein the procedures further comprise determining a ratio of integrated intensity of the fluorescent signals from the at least second fluorescent reporter molecule between the endoplasmic reticulum mask and the Golgi apparatus mask on and/or in the multiple cells.

61. (New) The machine readable storage medium of claim 30, wherein the cellular macromolecule of interest is a protein.

62. (New) The machine readable storage medium of claim 30, wherein the at least second fluorescent reporter molecule comprises a fluorescently labeled antibody.

63. (New) The machine readable storage medium of claim 30, wherein the multiple cells are fixed cells.

64. (New) The machine readable storage medium of claim 30, wherein the intensity of the fluorescent signals from the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells in response to contacting the cells at the first time point with the test stimulus is compared to the intensity of fluorescent signals of the at least second fluorescent reporter molecule within the mask of each of the two or more cellular compartments of interest on and/or in the individual cells in response to contacting the cells with the test stimulus from at least the second time point.

65. (New) The machine readable storage medium of claim 64, wherein the multiple cells are live cells.